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13. SUPPLEMENTARY NOTES
AFOSR Grant F49620-00-1-0334 was awarded to complete work begun under AFOSR Grant F49620-1-0246. This report includes data collected under the previous grant.

14. ABSTRACT During extended duration missions, Air Force pilots are exposed to markedly abnormal rest-duty cycles, leading to a loss of an appropriate phase relation between the 24-hr sleep/wake cycle and the endogenous circadian timing system. Misalignment of circadian phase is associated with sleep disruption and deterioration of alertness and cognitive performance, and can result in lapses of attention during the extended duty hours. To prevent such misalignment, development of effective non-pharmacological countermeasures are needed to facilitate adaptation of the human circadian pacemaker to the imposed duty-rest schedule. A study investigating the effects of exercise on physiologic adaptation to shiftwork and/or transmeridian travel under strictly controlled dim light was completed. Eighteen young, fit male subjects completed a 15-day protocol in which circadian phase was measured before and after exposure to a week of nightly bouts of exercise. Subjects who completed three 45-minute bouts of cycle ergometery each night showed a significantly greater shift in DLMOn_25% as compared to non-exercising controls (p=0.039). This finding has important implications for the treatment of circadian rhythm disorders, such as jet-lag and shift-work dyssomnia. Further investigation of the optimal timing of exercise is required to maximize the effectiveness of multiple nightly-bouts of exercise as a means of rapidly facilitating entrainment of the endogenous circadian pacemaker to abnormal sleep/wake cycles during operational contingencies.

15. SUBJECT TERMS

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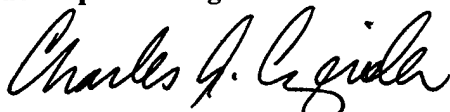
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FINAL REPORT

CLINICAL TRIAL OF EXERCISE ON CIRCADIAN CLOCK RESETTING

Grant Number: F49620-00-1-0334

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2. Objectives:
The objectives of this research effort were:

Specific Aim 1: test the hypothesis that a 9-hr phase delay shift of the duty-rest schedule, such as that required for either transmeridian travel or night operations, will induce physiologic maladaptation in the endogenous circadian rhythms of core body temperature, plasma melatonin, reaction time, alertness and performance;

Specific Aim 2: test the hypothesis that multiple nightly bouts of exercise will induce significant delays in the endogenous circadian rhythms of core body temperature, plasma melatonin, reaction time, alertness and performance relative to the control group, even in the absence of properly timed exposure to photic cues;

Specific Aim 3: test the hypothesis that exercise-induced phase delay shifts of will facilitate adaptation of these rhythms to an imposed duty-rest schedule, thereby improving sleep efficiency during daytime sleep and improve reaction time, alertness and performance during scheduled waketime at night relative to control group.

3. Status of Effort:
We impaneled and completed data collection on seven subjects in the grant period (6/5/00-10/31/00). Previously, we impaneled twelve research subjects and completed data collection on eleven of them (under prior AFOSR Grant F49620-97-1-0246). Thus, data from 18 subjects were included this report. The data collected during the 15-day study include: pre-study estimated oxygen uptake capacity, minute-by-minute samples of core-body temperature; hourly blood plasma samples; neurobehavioral testing including the reaction time task (psychomotor vigilance test) every two hours; nightly polysomnographic recordings; daily subjective assessments of sleep quality questionnaires; physiologic data from the 3 nightly exercise/control sessions for seven nights (monitoring heart rate, revolutions per minute (RPM), and perceived rate of exertion (RPE)), and urine samples collected every three waking hours. Analyses of body temperature and melatonin data are completed and are detailed in this report. The analysis of sleep and performance has begun, but is not yet completed. Some measures of these variables are included in this report; manuscripts of their complete analysis will be forwarded in the near future.

4. Accomplishments/New Findings:

Overview of Study Design
The purpose of this study was to test three specific hypotheses evaluating the ability of exercise to phase shift the human circadian pacemaker. These hypotheses were based on the results of preliminary data in human subjects and extrapolated from multiple lines of animal data which indicate that: (a) abnormal light-dark schedules, such as that following transmeridian travel or during night operations, result in the misalignment between the

endogenous circadian timing and the 24-hour work-rest cycle; (b) critically timed exposure to exercise is capable of producing phase shifts of the endogenous circadian activity rhythm in hamsters thus facilitating adaptation to imposed light-dark cycles; (c) critically timed exposure to exercise may be capable of inducing phase delay shifts of the endogenous circadian rhythms of temperature and melatonin in humans thus facilitating physiological adaptation to imposed work-rest schedules. A randomized clinical trial to test these hypotheses was completed.
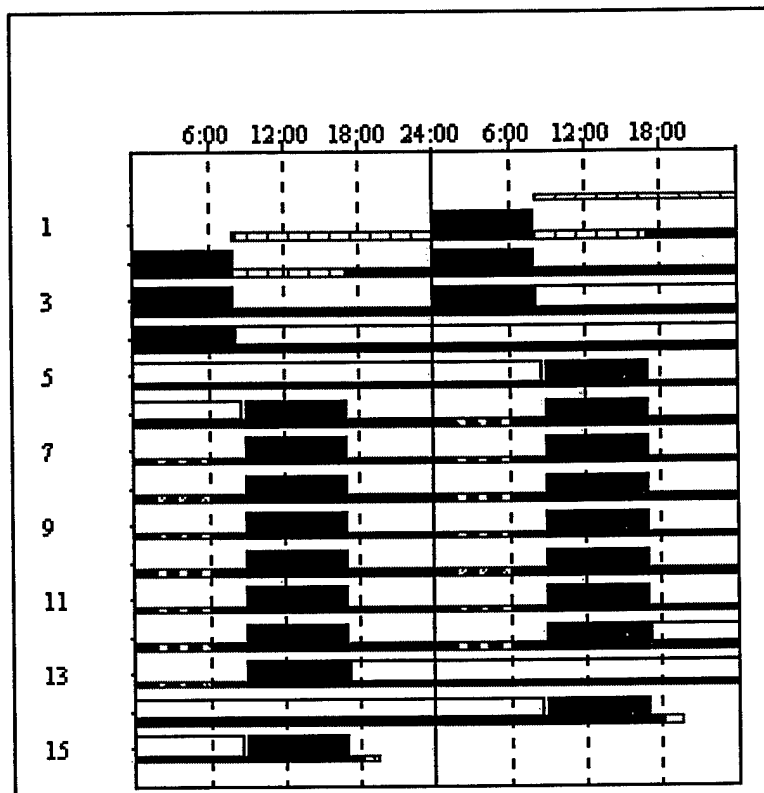

Figure 1. 15-day experimental protocol. Sleep episodes (8-hours) are shown as large black boxes. During the first baseline day the subject was exposed to 150 lux (thin open gray box with vertical lines). For the remainder of the study subjects were in the <5 lux condition (thin gray bar). Following the 3 baseline days, there was a 49-hour constant routine (large open gray box). The subject's sleep/wake schedule was then delayed by 9 hours. During the seven experimental days of the protocol, the 45-minute exercise/control bouts occurred nightly (small black boxes). A second CR (40 hours) was scheduled before the last sleep episode.

Upon admission to the study, subjects were acclimated with three baseline days (LD 16:8), where subjects continued to sleep and wake at their habitual times, followed by a constant routine to assess circadian phase. The subject's sleep/wake cycle was then delayed 9 hours for seven experimental days, where subjects were randomly assigned to either the exercise or control group. From Day 7 through 13, subjects underwent three 45-minute nighttime bouts of cycle ergometry (exercise group) or sitting on the cycle without peddling (control group). A second constant routine to assess final circadian phase followed the experimental treatment days. We anticipated that exposure to three 45-minute bouts of exercise scheduled to occur at night in the exercise group subjects would result in a significant delay phase shift of all circadian variables thus facilitating physiological adaptation to the new sleep/wake schedule. Furthermore, we anticipated that the endogenous rhythms of core body temperature, melatonin, reaction time, alertness and performance of subjects in the control group would drift with the approximate length of their individual period

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length, which is slightly longer than 24 hours.

Specific Methodology

<u>Subject Recruitment</u>. Healthy, fit, young men (aged 18-30 years) were recruited for participation in this study. Each potential subject underwent an extensive screening process and were required to be free from any acute, chronic or debilitation condition. Normality was established on the basis of clinical history, electrocardiogram (ECG), clinical biochemical screening of blood and urine, psychological questionnaires and psychological and physical examination. Finally, a symptom-limited maximal exercise test was given to each potential subject during the screening process. The test was administered on a treadmill using a Bruce protocol that increases speed and grade every 3 minutes (see Figure 2).

Minute	Speed (mph)	Grade (%)	Est VO2 max (ml/kg-min)
3	1.7	10	12.6
6	2.5	12	24.5
9	3.4	14	35.7
12	4.2	16	47.25
15	5	18	59.5
18	5.5	20	70

Figure 2. Bruce protocol for symptom-limited maximal treadmill test given to each potential subject during the screening process.

Heartrate, blood pressure and ECG was monitored throughout the treadmill test. The protocol continued until the subject fatigued and indicated he could not continue or until the subject exhibited adverse symptoms, such as abnormal ECG, decreased systolic BP, angina, or dyspnea. Healthy young men screened in for this study usually stopped due to fatigue localized in their legs, as the grade becomes quite steep for those not trained in hill running. Subjects that were able to complete 12 minutes of the treadmill protocol were eligible for this study.

<u>Ambulatory physiologic monitoring</u>. Subjects were required to maintain a regular, self-selected slee/wake schedule for three weeks prior to admission to this study. Compliance was monitored by evaluating a diary of sleep and wake times kept by the subjects. Subjects were also required to call into a date/time stamped answering machine just prior to going to bed and immediately upon awakening. Wrist activity and ambient light levels were monitored for 1 week immediately prior to admission to the laboratory with a solid-state, portable data collection device (Actiwatch-L; Minimitter; Bend, OR).

<u>Inpatient environment and conditions</u>. Upon admission to the study, subjects were isolated from external time cues, including clocks, radios, television, visitors, and sunlight, but maintained contact with staff members using techniques described elsewhere (10). Environmental temperature was maintained at 75 ± 3 °F. The experimental suites were equipped with hand-held terminals for on-line event recording, a porthole for 24-hour blood sample collection without disturbing the subject's sleep, and a closed-circuit camera and a voice-activated microphone for continuous subject

monitoring. Technicians and research nurses were present 24 hours a day to carry out the protocol, monitor the data acquisition systems, collect biologic specimen, and polygraphically record sleep episodes. Staff were trained to avoid communicating either the time of day or the nature of the experimental conditions to the subjects. An extensive series of written protocols and checklists were used to insure uniformity in the execution of standard procedures (e.g., at bedtime and wake time) and to foster intra-staff communications (e.g., at shift change).

Lighting. The experimental suites in the Intensive Physiological Monitoring Unit of the General Clinical Research Center have ceiling-mounted fluorescent fixtures that are controlled by a computer system. This system automatically turned the lighting on and off at the pre-determined wake and bedtimes to a pre-set intensity. During all sleep episodes, subjects were in darkness (<0.02 lux). During the first day of the protocol, the waking illumination level was that of normal indoor room light (~150 lux). During the constant routine and experimental portions of the study, the waking illumination was very dim. The lighting computer programming was changed during the course of this study; thus, the lighting level was not identical for every subject. Nevertheless, in all cases, light levels were very dim, always less than 5 lux and in most cases less than 1 lux. Mean light level for all subjects throughout the studies was 0.65±0.02 lux (see Appendix, Table 2).

Wake episodes. During wake episodes, the subjects were free to move about the suite as desired, except to lie down or nap. Subjects' activity was monitored for compliance by means of closed-circuit cameras.

Sleep and polysomnographic recording. Subjects were instructed not to get out of bed, even if they awakened before the end of the scheduled sleep episode. If requested, a technician brought the subject a urinal or bedpan during the scheduled sleep episode. Sleep episodes were polysomnographically recorded. Surface electrodes (Beckman Instrument Company, Schiller Park, IL) were applied to specific locations on the subject's face and scalp prior to bedtime for the recording of central (C3 and C4) and occipital (O1 and O2) electroencephalogram (EEG), electrooculogram (EOG: LOC and ROC), electromyogram (EMG, chin leads used), and electrocardiogram (ECG). All data were collected using the Nicolet Sleep/Wake Respiratory Analyzers (Nicolet Biomedical Instruments; Madison, WI) or the Vitaport 3 digital sleep recorders. The data were stored onto an 85 megabyte flash RAM card for downloading to a dedicated PC station after wake time and double archived onto CD/ROM.

Constant routine. To accurately assess endogenous circadian phase, each subject underwent two constant routines (CR). The initial CR was 49 hours and the final CR was 40 in length. The constant routine consisted of a regimen of enforced semi-recumbent wakefulness in constant indoor light, with nutritional intake divided into hourly aliquots, with activity restricted to prevent changes in body posture and activity level that could affect core body temperature. Core body temperature (each minute), blood samples

(every 30 minutes), and urine samples were collected throughout the constant routines. A technician was present at all times during the constant routines to ensure wakefulness.

Hormonal data. Samples of blood were collected every 60 minutes (sampling rate was increased to 30 minutes during constant routine portions of protocol) through an indwelling 18-gauge intravenous catheter located in a forearm vein. The catheter was connected to a triple-stopcock manifold (Cobe Laboratories Inc., Lakewood, CO) via an intravenous loop with a 12-foot small-lumen extension cable (Sorex Pharmaceuticals, Salt Lake City, UT) through which blood sampling continued in the next room without disturbing the subject during sleep. Between samples, a solution of 0.45% saline with 10,000 IU/liter of heparin was infused at a rate of 20 cc/hour to maintain patency. Blood samples were transferred to small (3 cc) vacutainer tubes and immediately centrifuged at 4°C; the resulting plasma or serum was pipetted into polystyrene tubes and frozen at -20°C until analysis. Melatonin assays were performed by Elias USA (Osceola, WI) using a radioimmunoassay with assay sensitivity of 2.5 pg/ml, with an intra-assay coefficient of variation of 8% and an interassay coefficient of variation of 13%. Saliva samples were collected hourly throughout all waking episodes for the purposes of melatonin assay in the event of difficulties with blood sampling. Since all melatonin blood assays were acceptable in all subjects, saliva assays were not performed.

Body Temperature. Core body temperature was continuously monitored by means of a rectal temperature sensor (Yellow Springs Instrument Company, Yellow Springs, OH). A real-time, online data acquisition system utilizing IBM-PC-compatible, pentium-based computers was employed to monitor and collect data.

Exercise Intervention. In subjects randomized to the exercise group, three 45-minute bouts of exercise separated by 1-hour rest periods were performed daily throughout the experimental portion of the protocol. The first exercise bout began 8.75 hours after waking and ended 9.50 hours after wake time. There was then a 1-hour rest period, followed by bout 2 from 10.50 until 11.25 hours after wake time. Another 1-hour rest period then occurred, followed by bout 3, from 12.25 until 13.00 hours after wake time. The overall duration of the exercise intervention, including rest periods, was 4.25 hours, occurring in the latter part of the waking day (centered 10.875 hours after waketime), and ending 3 hours before the start of the sleep episode (Figure 1).

During each exercise bout, subjects were required to maintain an intensity of 65-70% of their maximal heart rate (equivalent to approximately 50-55% of VO_2 max) pedaling at a rate of 65-70 revolutions per minute (RPM) on a bicycle ergometer (Cybex model 700R, Cybex, International Inc., Medway, MA) which is considered a moderate exercise level (Appendix, Table 3). Maximal heart rate values were determined from the symptom-limited maximal exercise test given to each potential subject during the screening process. A trained technician was present throughout all exercise interventions in the study to oversee each exercise bout, to measure blood pressure, to record heart rate and ergometer RPM every minute, to record rate of perceived exertion (RPE) and to ensure

that the target exercise intensity was achieved. The technician also instructed the subject in leg stretching exercises prior to and after each exercise intervention

Subjects randomized to the control group underwent the same protocol, including pre- and post-exercise stretching procedures, at the same relative clock hour and for the same durations. However, control subjects only sat on the ergometer (to control for posture) but did not pedal. A technician was present to supervise all control sessions.

Neurobehavioral Testing. During all waking hours throughout the in-laboratory portions of the protocol, subjects completed computer-administered neurobehavioral test batteries at frequent intervals. Tests that have been shown to vary with circadian phase and sleep loss and tests that do not show strong or long-lasting training effects (PVT, KSS and VAS) were chosen for this battery.

Sustained attention performance was assessed using the Psychomotor Vigilance Test (PVT) of Dinges and Powell (5). The PVT was a test of visual reaction time (RT) in which the subject was asked to maintain the fastest possible RTs to a simple visual stimulus for a task duration of 10 minutes. The inter-stimulus interval involved a high signal rate randomly varying between 2 and 10 seconds. A variety of performance metrics showing stable circadian variation were obtained from each PVT trial including the number of lapses, optimum response times, false alarms, and the characteristics of vigilance decrement functions (i.e., slope, y-intercept) as a result of time on task. Different transforms applied to variables reduced inter-subject variability and provided stable estimates of circadian variation.

A Calculation Performance task, modeled after one described by Klein et al. (8) presented the subject with a series of randomly generated pairs of 2-digit numbers. The subject's task was to sum as many pairs as possible in the allotted four-minute time interval. The test, a measure of cognitive throughput, was scored according to the number of calculations completed in the time allowed, as well as the accuracy.

The Karolinska Sleepiness Scale (KSS) assessed subjective sleepiness/alertness, and required the subject to select a number on a scale from 1 to 9 spanning the range from very sleepy to very alert.

Visual Analogue Mood and Alertness Scales (VAS) were used to measure subjective mood and sleepiness/alertness (2;4;7). The scales consisted of a horizontal line drawn on the computer display with each end of the line labeled with the extremes of a subjective continuum, e.g. happy-sad, or sleepy-alert. Subjects indicated a position on the line that best described how they felt at that moment.

A Post-Sleep Questionnaire (PSQ) was completed immediately following wake time from all sleep episodes in the laboratory and provided information on subjective evaluation of sleep onset, duration, consolidation, quality, and wakefulness during sleep.

Statistical analysis

Melatonin phase. Plasma samples collected under dim light conditions were analyzed for melatonin to determine circadian phase. The time at which the rising portion of the plasma melatonin curve crossed a level that was 25% of the peak value of the curve (6) was defined as the melatonin onset (DLMOn_25%). Dim light melatonin offset (DLMOff_25%) was defined to be the time at which the falling portion of the interpolated plasma melatonin curve crossed a level that is 25% of the peak value of the curve (6). The mean point between the DLMOn_25% and the DLMOff_25% was defined as the midpoint of the melatoinin curve.

Melatonin phase was analyzed for each day of the protocol during which plasma samples were collected (Day 2 through end of study). These daily melatonin phase estimates provided analysis of the day-to-day progression of phase shifts in all subjects. The DLMOn_25% measured on CR2 was compared to the DLMOn_25% measured during CR1 to determine the phase shift each subject achieved.

Body Temperature. An estimate of the circadian phase (timing of body temperature minimum) and amplitude of the core body temperature data collected was made using a dual harmonic regression model (3). The timing of the body temperature phase on CR2 was compared to the body temperature phase measured during CR1 to determine the shift each subject achieved.

Polynomnographic sleep recordings. Sleep was recorded each night throughout the protocol, and sleep recordings were scored visually in 30-second epochs according to the method of Rechtschaffen and Kales (9). Each sleep episode was analyzed for sleep efficiency (total sleep time divided by total time in bed). Further sleep analysis is ongoing with each sleep episode being analyzed for latency to sleep onset (minutes), and wake after sleep onset (WASO; minutes).

The first 3 days of the protocol served to ensure that the circadian pacemaker of all subjects was stably entrained and allowed subjects to adapt to the laboratory conditions, both of which were important in the evaluation of baseline sleep quality. Due to the well-known "first-night" effect of sleep disruption from sleeping in a new environment (1), the average of nights 2 and 3 were used as the baseline conditions for each subject. The seven nights of sleep during the experimental segment of the protocol were compared to the baseline sleep to determine whether changes in sleep variables occur over the course of the protocol. Night by night measurements between the exercise and control subjects were analyzed.

Neurobehavioral Testing. Each of the tests was administered automatically by computer at frequent intervals and initial processing of test results were calculated automatically (exact time of administration; scoring of mood and alertness tests; number and accuracy of additions completed on the ADD; mean and median reaction time, number of lapses, and shortest and longest reaction times on PVT). To account for inter-subject variability on these tests, each subject's scores were referenced to his/her mean value and

normalized in terms of variability (Z-scored) using the data from the baseline days. Data from each individual were analyzed with respect to time-since-waking for each day of the study, and data were compared between the exercise and control groups.

Results

Eighteen males (23.0 ± 0.2 years; Mean ± SEM) completed the 15-day protocol; each was randomly assigned to either the control or exercise group (see Appendix, Table 1).

<u>Melatonin</u>. Data from the pre- and post-experimental intervention CRs were assessed to determine whether repetitive, nightly bouts of exercise elicited significant phase delay shifts of the endogenous circadian melatonin rhythm. It was anticipated that over the nine intervening 24-hr-cycles between the pre- and post CR assessments in dim light, the endogenous circadian pacemaker of the nine subjects studied under the control conditions would drift with an average intrinsic period of ~24.18-hr, which would result in an observed phase delay shift of the endogenous circadian melatonin rhythm of ~1.8-hr. Indeed, analysis of the DLMOn_25% from the control condition revealed mean ± SEM phase delay shifts of 1.67 + 0.51-hr. In contrast, examination of the data from the nine subjects in the exercise condition revealed a mean DLMOn_25% ± SEM phase shift of 3.17 + 0.74-hr in the plasma endogenous melatonin rhythm. Thus, the exercise group showed a significantly (p=0.039) greater phase shift with this protocol suggesting that exercise can significantly facilitate circadian adaptation to night shift work and jet lag (Figure 3).
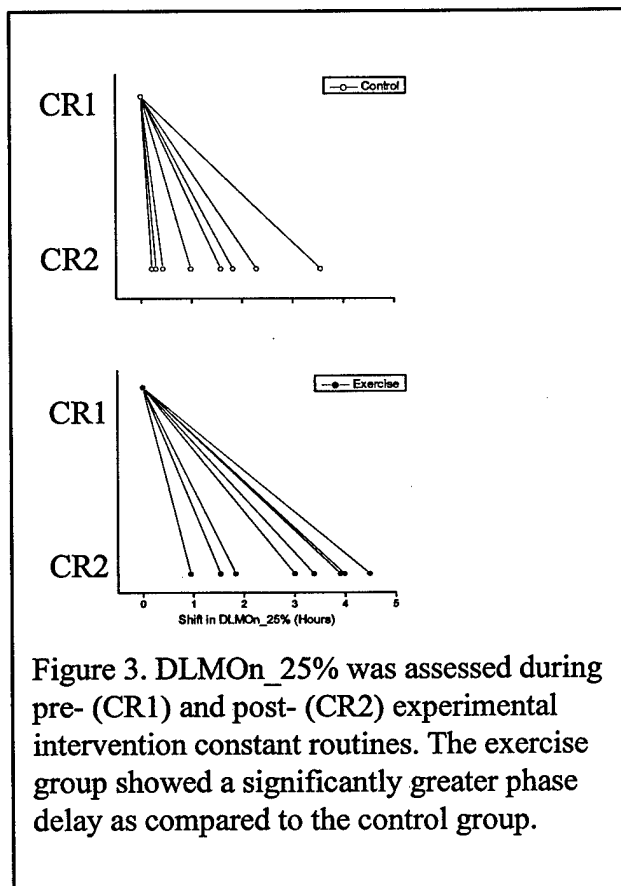

Figure 3. DLMOn_25% was assessed during pre- (CR1) and post- (CR2) experimental intervention constant routines. The exercise group showed a significantly greater phase delay as compared to the control group.

Since this protocol scheduled the midpoint of the experimental intervention 10.875 hours after waketime, it occurred at a different relative point in the circadian cycle (as measured by DLMOn_25%) for each subject. The amount of phase delay induced by the exercise intervention was significantly dependent on the relative timing of the exercise with respect to the pre-intervention DLMOn_25% (r=-0.73, p=0.025). Figure 4 illustrates the relationship between the relative timing of the intervention (exercise and control) with respect to the pre-intervention DLMOn_25% and the magnitude of the phase shift produced by the intervention. Exercise centered approximately four hours after the pre-
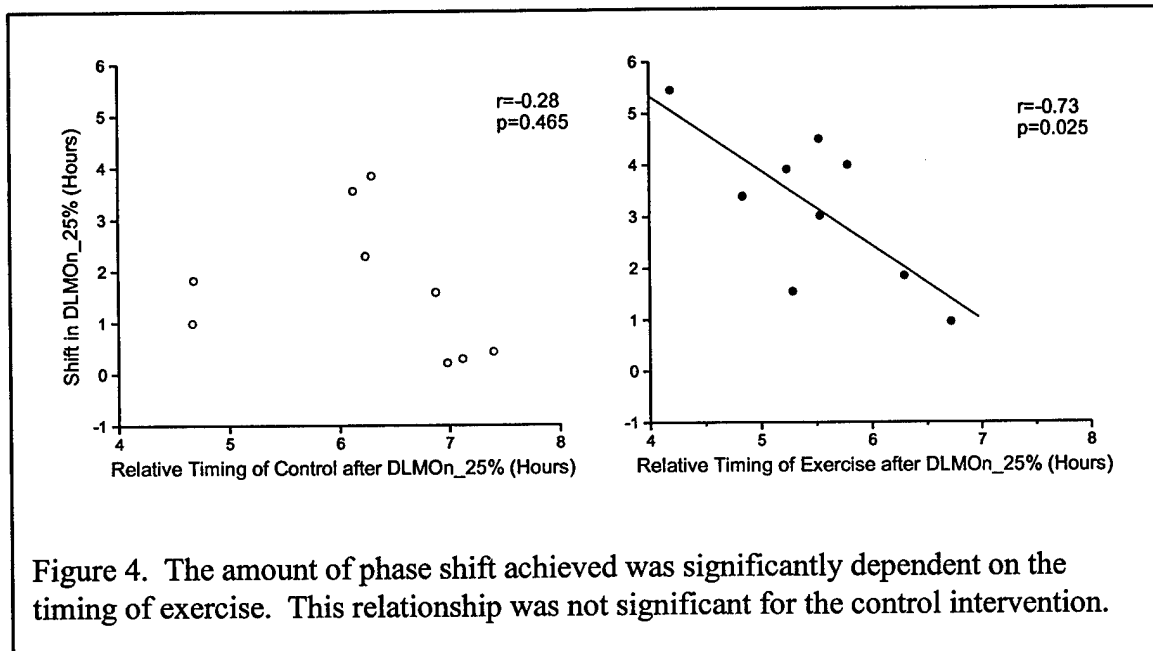
Figure 4. The amount of phase shift achieved was significantly dependent on the timing of exercise. This relationship was not significant for the control intervention.

intervention DLMOn_25% elicited the largest phase delay. The later the exercise was performed following the DLMOn_25%, the less of a phase shift that was produced. This relationship did not hold true for the control group. In other words, the timing of the control session, with the subject sitting on the bike, but not pedaling, and the amount of phase shift produced was not significantly related (r=-0.28; p=0.465). Thus, the association between the timing of DLMOn_25% and the phase shift produced was not merely due to the intervention itself, but specifically related to exercise. In summary, these data suggest that exercise must be properly timed to significantly phase delay the human circadian pacemaker and thereby facilitate circadian adaptation to schedules requiring a delay in the sleep/wake schedule.

Body Temperature. Similar to melatonin data analysis, the timing of the endogenous body temperature rhythm was compared between the pre-experimental intervention CR (CR1) and the post-intervention CR (CR2) to assess the effect of repetitive, nightly bouts of exercise on the endogenous circadian body temperature rhythm. Again, it was expected that during the nine intervening 24-hr-cycles between the pre- and post CR assessments in dim light, the endogenous circadian pacemaker of the nine control subjects would drift with an average intrinsic period of ~24.18-hr, resulting in an observed phase delay shift of the endogenous circadian body temperature rhythm of ~1.8-hr. In fact, the control subjects averaged delay shifts of 2.22 ± 0.19 hr (Mean ± SEM). Two of the subjects in the exercise group were unable to be used in the body temperature analysis. One subject (19d3c) was not able to continue using the rectal temperature sensor following CR1. Another subject's (1308cx92) endogenous body temperature rhythm amplitude was too low (<0.25 °C) to accurately determine circadian phase. The mean (± SEM) phase shift of the body temperature rhythm in the exercise group was 2.85 ± 0.13 hr. (See Appendix, Table 4). The difference in the phase shift achieved between the exercise and control group was not significant, and the evaluation as to whether exercise can delay the circadian rhythm of body temperature is inconclusive. Due to the higher

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variation in body temperature compared to melatonin data and effectively fewer subjects in the exercise group, almost three times as many subjects (18 in each group) would have been needed to have a 95% chance of detecting a difference in the phase shift. Thus, we did not have the power to detect whether or not exercise could induce a change in circadian phase using body temperature as a phase marker.

Sleep. All sleep episodes for five control subjects and six exercise subjects were visually scored in 30-second epochs. Sleep efficiency was calculated for each sleep episode as total sleep time divided by the total time in bed. Baseline sleep efficiency was calculated for each subject by averaging the sleep efficiency of the second and third night of the protocol. Sleep efficiency on the seven experimental nights will be compared to baseline for each subject and changes in sleep efficiency between the exercise and control group will be analyzed. Evaluation of significant statistical differences awaits completion of the sleep scoring. However, results of the first eleven subjects look encouraging and appear to suggest that exercise ending three hours before a scheduled sleep episode imposes no adverse effects on sleep.

Neurobehavioral Testing. Analysis of neurobehavioral testing is not completed.

Conclusions.
It has been demonstrated in animals that physical activity is capable of acutely shifting the output of the circadian pacemaker. Previous studies using human subjects suggested that exercise may elicit similar results, although lighting conditions were not closely controlled in those studies. This recently completed study investigated the effects of exercise on physiologic adaptation to shiftwork and/or transmeridian travel under strictly controlled dim light. Eighteen young, fit male subjects completed a 15-day protocol in which circadian phase was measured before and after exposure to a week of nightly bouts of exercise. Subjects who completed three 45-minute bouts of cycle ergometery each night showed a significantly greater shift in DLMOn_25% as compared to non-exercising controls (p=0.039). This finding has important implications for the treatment of circadian rhythm disorders, such as jet-lag and shift-work dyssomnia, both common conditions in Air Force pilots. Further investigation of the optimal timing of exercise is required to maximize the effectiveness of multiple nightly-bouts of exercise as a means of rapidly facilitating entrainment of the endogenous circadian pacemaker to altered sleep/wake cycles during operational contingencies.

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5. Personnel Report:

Charles A. Czeisler, Ph.D., M.D.	Professor of Medicine
Laura Barger, Ph.D.	Post Doctoral Fellow in Medicine
Rod Hughes	Instructor in Medicine
David Rimmer	Graduate Student
Conor O'Brien	Research Assistant

6. Publications:

Manuscripts reporting on this study are in preparation.

7. Interactions/Transitions

A. Participation/presentations:
A presentation of these data is scheduled for May 15, 2001 during the Providence Sleep Research Interest Group meeting at Brown University, Providence, R.I.

B. Consultative and advisory functions:
Dr. Barger is consulting with the Air Combat Command (ACC) on fatigue countermeasures. She has written an educational module on the effects of exercise on circadian rhythmicity to be incorporated into ACC Sustained Operations Fatigue

Countermeasures CD.

C. Transitions:
Data from these experiments will be incorporated into a model of alertness and
performance currently being developed to counteract fatigue associated with Air Force
missions. The model is being developed through the support of the AFOSR Partnership
for Research Excellence and Transition Program (PRET), Center on Countermeasures for
Jet Lag and Sleep Deprivation organized at the University of Pennsylvania.

8. New discoveries, inventions, or patent disclosures:
None

9. Honors/Awards:

LK Barger: National Research Service Award, Training in Sleep,Circadian, and
Respiratory Neurobiology, 2000-2001

APPENDIX

Subject Number	Condition	Admit Date	Age
1827c	Exercise	10-Feb-98	24
1828c	Exercise	27-Feb-98	25
1847c	Control	30-Mar-98	18
1857c	Control	8-May-98	20
1856c	Exercise	23-May-98	25
1877c	Control	7-Jun-98	20
1975c	Control	4-May-99	30
1308cx92	Control	19-May-99	29
19c2c	Control	11-Aug-99	22
1997c	Exercise	13-Aug-99	20
19d3c	Control	9-Sep-99	28
2050c	Exercise	19-Jun-00	24
2052c	Exercise	26-Jun-00	20
2053c	Exercise	3-Jul-00	25
2068c	Control	27-Jul-00	21
2076c	Exercise	5-Aug-00	19
2084c	Exercise	22-Aug-00	20
19c30T2c	Control	8-Sep-00	24

Table 1. Subjects completing the 15-day exercise study.

Subject	Daily Mean Light Level (Lux)
1827c	1.00
1828c	1.02
1856c	0.74
1997c	1.02
2050c	0.67
2052c	0.26
2053c	0.31
2076c	0.27
2084c	0.24
1847c	1.02
1857c	1.29
1877c	0.79
1975c	0.68
19d3c	0.72
19c2c	0.60
1308cx92	0.48
2068c	0.35
19c30T2	0.23

Table 2. Mean light levels during 15-day study by subject.

		Stress Test	Avg % Max HR (Ex Sessions)		
Number	Condition	Max HR	1	2	3
1827c	Exercise	202	65	66	65
1828c	Exercise	207	64	65	65
1856c	Exercise	202	66	67	67
1997c	Exercise	204	61	62	65
2050c	Exercise	202	67	67	67
2052c	Exercise	183	73	74	75
2053c	Exercise	140	84	83	78
2076c	Exercise	176	67	66	66
2084c	Exercise	186	73	73	73
Mean			68.89	69.22	69.00
St Dev			6.88	6.40	4.97

Table 3. Mean percentage of maximum HR (determined from symptom limited maximal treadmill test administered pre-study) for exercise sessions by subject.

Number	Condition	Phase Shift in Tb (Hours)
1847c	Control	3.37
1857c	Control	2.57
1877c	Control	0.24
1975c	Control	-0.05
19d3c	Control	-
19c2c	Control	1.9
2068c	Control	4.96
1308cx92	Control	-
19c30T2c	Control	2.54
1827c	Exercise	4.02
1828c	Exercise	3.01
1856c	Exercise	3.75
1997c	Exercise	2.09
2050c	Exercise	1.66
2052c	Exercise	1.22
2053c	Exercise	1.85
2076c	Exercise	3.66
2084c	Exercise	4.39
	Exercise	**Control**
Mean	2.85	2.22
St Dev	1.17	1.74
sem	0.130	0.25

Table 4. Phase shift in body temperature minimum by subject.